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REGULAR ARTICLE

Arsenic speciation analysis of urine samples from individuals living in an arsenic-contaminated area in Bangladesh

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Abstract
Objectives Chronic inorganic arsenic (iAs) exposure currently affects tens of millions of people worldwide. To accurately determine the proportion of urinary arsenic metabolites in residents continuously exposed to iAs, we performed arsenic speciation analysis of the urine of these individuals and determined whether a correlation exists between the concentration of iAs in drinking water and the urinary arsenic species content.
Methods The subjects were 165 married couples who had lived in the Pabna District in Bangladesh for more than 5 years. Arsenic species were measured using high-performance liquid chromatography and inductively coupled plasma mass spectrometry.
Results The median iAs concentration in drinking water was 55 μgAs/L (range <0.5–332 μgAs/L). Speciation analysis revealed the presence of arsenite, arsenate, monomethylarsonic acid (MMA), and dimethylarsinic acid in urine samples with medians (range) of 16.8 (7.7–32.3), 1.8 (<0.5–3.3), 13.7 (5.6–25.0), and 88.6 μgAs/L (47.9–153.4 μgAs/L), respectively. No arsenobetaine or arsenocholine was detected. The concentrations of the 4 urinary arsenic species were significantly and linearly related to each other. The urinary concentrations of total arsenic and each species were significantly correlated with the iAs concentration of drinking water.
Conclusions All urinary arsenic species are well correlated with each other and with iAs in drinking water. The most significant linear relationship existed between the iAs concentration in drinking water and urinary iAs + MMA concentration. From these results, combined with the effects of seafood ingestion, the best biomarker of iAs exposure is urinary iAs + MMA concentration.

Keywords Arsenic · HPLC-ICP-MS · Speciation analysis · Urine · Drinking water

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Introduction

In Bangladesh, the United Nations International Children's Emergency Fund (UNICEF) and other nongovernmental organizations encouraged a massive shift from drinking microbially contaminated surface water to groundwater accessed by tube wells to reduce infant mortality associated with diarrheal diseases in the 1960s. In the 1990s, it was discovered that roughly one-half of these wells contained high concentrations of arsenic [1, 2]. Since then, many epidemiological studies have been conducted. We previously reported the relationship between inorganic arsenic (iAs) concentrations in well water and the total urinary

arsenic concentrations of residents living in the Pabna District of Bangladesh—an area in which groundwater is contaminated by arsenic—to examine the effectiveness of the arsenic mitigation program [3]. We found that green-marked wells, which the Bangladesh government regards as safe, are not always safe.

The International Agency for Research on Cancer (IARC) concludes that there is sufficient epidemiological evidence for the toxicity of iAs in humans such as carcinogenicity of the lungs, skin, and urinary bladder [4]. Methylation of iAs to monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) has been demonstrated in humans and several mammalian species [5]. These metabolites are less reactive in tissue constituents than iAs and are readily excreted in urine. However, reactive intermediates of trivalent MMA and DMA (MMA^{III} and DMA^{III}) produced in iAs metabolic processing in mammals may be responsible for the observed carcinogenic effects [6–9]. Therefore, in 2010, the IARC classified MMA and DMA as group 2B compounds, and arsenobetaine (AsBe) and other organic arsenic compounds that are not metabolized in humans as group 3 compounds [10]. Since toxicities of arsenic-based compounds vary greatly due to their different chemical configurations, relative proportions of urinary metabolites of iAs have been identified as potential biomarkers of susceptibility to iAs toxicity [5, 11–13]. Recently, chemical speciation analysis using high-performance liquid chromatography with inductively coupled plasma mass spectrometry (HPLC-ICP-MS) has been used to monitor iAs exposure. Because HPLC-ICP-MS analysis can determine whether subjects have ingested seafood and the presence or absence of arsenic metabolites more precisely than hydride generation atomic absorption spectrophotometry (HG-AAS), HPLC-ICP-MS is indispensable for biological monitoring of residents exposed to iAs.

Speciation analysis of urinary arsenic has been conducted among populations who drink arsenic-polluted water [14–16]; however, the relationships between each urinary arsenic species are not reported. To accurately determine the proportions of urinary arsenic metabolites of individuals continuously exposed to iAs, we performed arsenic speciation analysis of the urine of residents drinking iAs-contaminated water who do not ingest organic arsenic from seafood. We used HPLC-ICP-MS to examine the relationships between urinary arsenic speciation levels and iAs concentrations in drinking water.

Materials and methods

Subjects

The subjects were residents of 17 villages in the Pabna District in Bangladesh, which is located northwest of the capital city of Dhaka [3]. Inhabitants of these villages are entirely dependent on the water supplies of tube wells that were installed by individual households, the government, or nongovernmental organizations. Subjects were chosen from volunteers gathered through community recruitment in this area. We recruited families that had lived in the area for at least 5 years before recruitment in which the husband had not engaged in seasonal or long-term migratory jobs. Of the families satisfying these entry criteria, approximately one-third of the families in the study area were enrolled. The subjects included 330 residents (165 married couples; 165 males and 165 females) who did not customarily eat seafood. Their profiles are shown in Table 1. Informed consent was obtained from the subjects. The study protocol was approved by the Ethics Committee of Osaka City University Graduate School of Medicine. After the field procedure was discussed, the Civil Surgeon's office of Pabna District gave permission for research activity in this area. Drinking water concentration is expressed according to the well water concentration for each subject used. When a subject drank water from 2 different wells, the average concentration was used. Water and urine samples were collected in the mornings between May and July 2005 and kept frozen at −20°C at a laboratory in Bangladesh and at −80°C at a laboratory in Japan.

Chemicals

Sodium arsenite (AsIII), sodium arsenate (AsV), MMA, and AsBe were purchased from Wako Pure Chemical Industries (Osaka, Japan). DMA, trimethylarsine oxide (TMAO), and arsenocholine (AsCho) were obtained from Tri Chemical Laboratory (Yamanashi, Japan). Germanium standard solution (Kanto Chemical, Tokyo, Japan) was used as an internal standard. HNO_3 (Tama Chemicals, Tokyo, Japan), NH_4NO_3 (Wako Pure Chemical, Osaka, Japan), and 2,6-pyridinedicarboxylic acid (Tokyo Kasei Industry, Tokyo, Japan) were used for the HPLC mobile phase. Ultrapure water for analysis was prepared using a Milli-Q Element A-10 with a Quantum ICP cartridge (Millipore Japan, Tokyo, Japan).

Analytical conditions

Untreated water samples were obtained and analyzed using ICP-MS as described in our previous report [3].

Total arsenic in urine samples was quantified using an Elan DRCII ICP-MS (PerkinElmer SCIEX, Concord, ON, Canada) under the following conditions: radiofrequency (RF) power 1300 W, gas flow—plasma 15 L/min, auxiliary flow 1.2 L/min, nebulizer flow 1.0 L/min, with platinum sample and skimmer cones. The dynamic reaction cell

Table 1 Distribution of age, BMI, iAs in drinking water, urinary tAs, sumAs, and urinary creatinine concentrations among 165 married couples

	Age (years)	BMI (kg/m^2)	iAs in drinking water (μgAs/L)	Urinary tAs[a] (μgAs/L)	Urinary sumAs[b] (μgAs/L)	Urinary creatinine (g/L)	Urinary sumAs (μgAs/g creatinine)
Total (330)							
Minimum	20	12.9	1	3.8	2.0	0.03	28.4
25 percentile	30	18.7	25	55.6	62.0	0.23	177.1
Median	37	20.0	55	118.6	126.1	0.41	323.3
75 percentile	46	22.2	86	200.0	222.2	0.61	541.5
Maximum	77	32.0	332	2166.0	2106.5	2.46	3420.1
Male (165)							
Minimum	24	14.8	1	13.0	14.9	0.05	28.4
25 percentile	35	18.6	25	63.6	68.3	0.30	149.8
Median	40	19.8	55	124.2	129.2	0.47	278.4
75 percentile	50	21.7	86	202.8	226.6	0.73	477.2
Maximum	77	27.9	332	874.7	1024.9	2.16	2507.3
Female (165)							
Minimum	20	12.9	1	3.8	2.0	0.03	33.4
25 percentile	27	18.7	25	43.3	48.6	0.18	209.1
Median	33	20.4	55	109.5	124.0	0.30	369.3
75 percentile	42	22.4	86	196.8	214.6	0.52	614.9
Maximum	61	32.0	332	2166.0	2106.5	2.46	3420.1
Median difference (p)	<0.001	0.086		0.368	0.582	<0.001	0.001

Median difference between males and females tested by Mann–Whitney U test. $p < 0.05$ is statistically significant

[a] Values are total arsenic concentrations directly determined by ICP-MS

[b] Values are concentrations of sum of arsenic compounds detected in speciation analysis

(DRC) mode of operation was set with ammonia (NH_3) as the reaction gas; the rejection parameter q (RPq) of the DRC and the flow rate of NH_3 were optimized and set to 0.5 and 0.3 mL/min, respectively. For total arsenic analysis, urine samples were diluted 10-fold with an aqueous solution containing 0.5% HNO_3 (TAMA PURE-AA-10; Tama Chemicals Co. Ltd., Tokyo, Japan), 0.5 g/L ethylenediaminetetraacetic acid (EDTA) (Titriplex II; Merck, Darmstadt, Germany), and 0.5 g/L Triton X-100 (Acros Organics, Geel, Belgium). Nonspectral matrix effects observed when DRC was used were confirmed by using NaCl at $m/z = 77$ for ArCl monitoring. The detection limit for arsenic was 0.24 μg/L.

Speciation analysis of urinary arsenic was performed using HPLC-ICP-MS as described in our previous report [17]. Although MMA and DMA exist in 2 different valence states (i.e., trivalent and pentavalent), we did not attempt to distinguish valence states in this study. This analytical procedure was validated using certified reference urine for internal quality control (NIES CRM No. 18 Human Urine; National Institute for Environmental Studies, Japan) and by using the external quality assessment program of the German External Quality Assessment Scheme (Institute of Occupational Social and Environmental Medicine of the University of Erlangen, Nuremberg, Germany) as described in our previous reports [17, 18].

Sample preparation

Frozen urine samples were thawed to room temperature and centrifuged at 3000 rpm for 10 min, and the resultant supernatants were used for analysis. The supernatants were diluted 10-fold with ultrapure water and analyzed using HPLC-ICP-MS as described above.

Statistical analysis

Data collected by questionnaire and urine measurements were analyzed using the SPSS statistical package (PASW SPSS Statistics 18; IBM Japan, Tokyo, Japan). A correlational analysis among urinary concentrations of arsenic species was performed with $\log_{10}$-transformed values. The median difference was tested using the Mann–Whitney U test.

Results

The distributions of age; body mass index (BMI); urinary total arsenic (tAs) concentration; the sum of concentrations of all arsenic compounds detected in urine by using HPLC-ICP-MS, including unidentified arsenic compounds (sumAs); iAs in drinking water; and urinary creatinine

concentrations among the 165 couples are shown in Table 1. Age and urinary creatinine concentration in females were significantly lower than those in males. Inversely, urinary sumAs concentration adjusted for creatinine in females was significantly higher than that in males. Urinary creatinine concentrations ranged from 0.03 to 2.46 g/L; the medians for males and females were 0.47 and 0.30 g/L, respectively. Creatinine values were significantly lower than those of Western people [19, 20]. Next, we analyzed urinary arsenic concentrations without adjusting for creatinine. Urinary sumAs concentrations ranged from 2.0 to 2106.5 μgAs/L; the distribution was similar for both sexes. There was good linear agreement between tAs and sumAs: $y = 1.07x + 4.55$ (where y = sumAs concentration, x = tAs concentration, $r = 0.996$).

In speciation analysis, AsIII, AsV, MMA, and DMA were detected in urine samples, whereas AsBe, TMAO, and AsCho, which are generated as a result of seafood ingestion, were not detected, as shown in Fig. 1. The medians (range) of AsIII, AsV, MMA, and DMA were 16.8 μgAs/L (7.7–32.3 μgAs/L), 1.8 μg/L (0.5–3.3 μgAs/L), 13.7 μg/L (5.6–25.0 μgAs/L), and 88.6 μgAs/L (47.9–153.4 μgAs/L), respectively. The proportion of each species as well as the methylation indices, the primary methylation index (PMI) of MMA/(AsIII + AsV) and the secondary methylation index (SMI) of DMA/MMA, are shown in Table 2. The most excreted arsenic compound

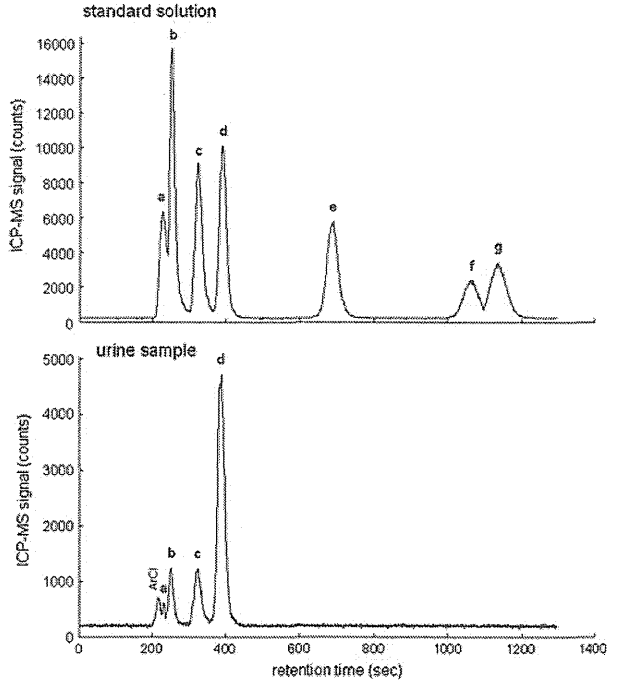

Fig. 1 Chromatograms of a standard solution and urine sample obtained using HPLC-ICP-MS. The peaks show: *a* AsV, *b* MMA, *c* AsIII, *d* DMA, *e* AsBe, *f* AsCho, and *g* TMAO

was DMA, accounting for approximately 70% of the total. Significant differences were observed between sexes in the proportions of arsenic species except DMA and iAs + MMA, and methylation indices. The proportion of MMA was significantly higher in males than in females; however, those of AsIII, AsV, and iAs in males were significantly lower than those in females. The SMI value was nearly 10 times greater than that of PMI in both sexes. PMI values in males were significantly higher than those in females, whereas SMI values were significantly lower than those in females.

Urinary arsenic species concentrations were $\log_{10}$-transformed; the relationship between each species is shown in Fig. 2. All regressions among the 4 species were significantly positive with Pearson's correlation coefficients (r) ranging from 0.6 to 0.9; the most strongly correlated relationship was obtained between log(MMA) and log(DMA) (Table 3). Moreover, log(iAs + MMA) exhibited significant positive linear relationships both with log(DMA) and log(sumAs) with r values of 0.92 and 0.96, respectively (Table 3).

The regression analysis between arsenic in drinking water and urinary arsenic species is shown in Fig. 3, and related equations are shown in Table 4. All urinary arsenic species were well correlated with arsenic in drinking water with correlation coefficients from 0.50 to 0.61. The relationship between urinary iAs + MMA concentration with arsenic in drinking water exhibited the best linearity. Concentrations of iAs + MMA and sumAs against 50 μgAs/L drinking water were estimated to be 35.4 and 132.7 μgAs/L, respectively.

The effects of iAs concentration in drinking water, BMI, urinary creatinine concentration, and age on the proportion of arsenic species and methylation indices were examined. Table 5 shows clear differences in arsenic effects with respect to sex. Concentration of iAs in drinking water was positively correlated with PMI but negatively with SMI; statistical significance was observed in males and totals but not in females alone. BMI was negatively correlated with MMA (%) and PMI, and statistical significance was observed in females and totals but not in males alone. Creatinine exhibited no significant effect for either sex. Age was significantly positively correlated with PMI but not SMI in both sexes.

Discussion

This study determined the relationships among species of urinary arsenic in residents drinking arsenic-polluted water. Distribution and correlation analyses revealed strong correlations between the $\log_{10}$-transformed concentrations of each arsenic species exceeding 0.8, except regarding the

Table 2 Proportion of urinary arsenic species and methylation indices among 330 subjects

	Proportion (%)						Methylation indices	
	AsIII	AsV	MMA	DMA	iAs[a]	iAs + MMA	PMI	SMI
Total (330)								
25 percentile	10.4	0.9	8.2	68.0	12.0	22.1	0.51	4.95
Median	13.4	1.5	10.9	73.2	15.4	26.7	0.68	6.65
75 percentile	16.5	2.3	13.9	77.8	18.9	31.7	1.00	9.25
Male (165)								
25 percentile	9.9	0.7	9.2	68.3	11.3	21.9	0.63	4.56
Median	12.6	1.2	12.2	73.5	13.9	26.5	0.84	6.03
75 percentile	15.7	1.8	15.2	78.1	17.0	31.5	1.10	8.41
Female (165)								
25 percentile	11.1	1.2	7.6	67.7	13.0	22.2	0.46	5.53
Median	14.6	1.8	10.0	73.0	16.8	26.8	0.59	7.10
75 percentile	17.6	2.7	12.7	77.7	19.9	32.2	0.77	10.03
Median difference (p)	0.001	<0.001	<0.001	0.912	0.001	0.912	<0.001	0.011

Median difference between males and females tested by Mann–Whitney U test. $p < 0.05$ is statistically significant

PMI primary methylation index calculated from urinary MMA/iAs, *SMI* secondary methylation index calculated from urinary DMA/MMA

[a] Values are sum of AsIII and AsV

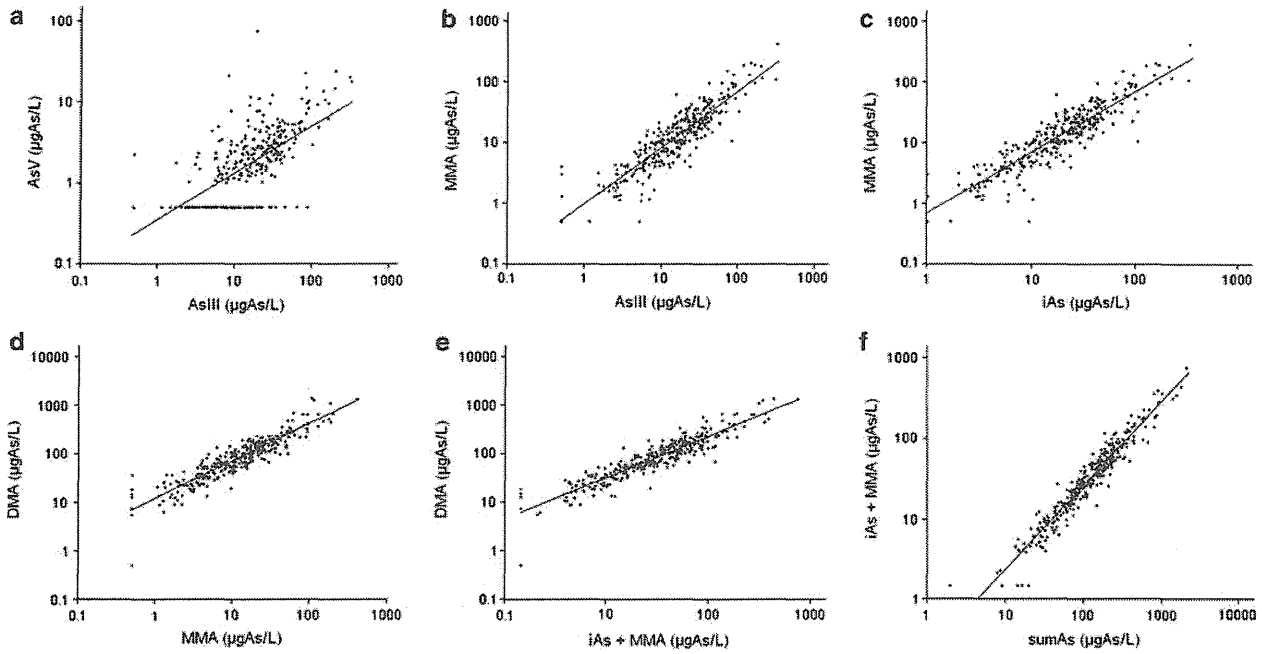

Fig. 2 Relationship between each arsenic species present in urine. **a** Relationship between AsIII (x) and AsV (y), $\log y = 0.578 \log x - 0.456$ ($r = 0.654$, $p < 0.0001$). **b** Relationship between AsIII (x) and MMA (y), $\log y = 0.923 \log x - 0.002$ ($r = 0.897$, $p < 0.0001$). **c** Relationship between iAs (x) and MMA (y), $\log y = 0.994 \log x - 0.151$ ($r = 0.902$, $p < 0.0001$). **d** Relationship between MMA (x) and DMA (y), $\log y = 0.772 \log x + 1.083$ ($r = 0.902$, $p < 0.0001$). **e** Relationship between iAs + MMA (x) and DMA (y), $\log y = 0.858 \log x + 0.647$ ($r = 0.921$, $p < 0.0001$). **f** Relationship between sumAs (x) and iAs + MMA (y), $\log y = 1.038 \log x - 0.658$ ($r = 0.962$, $p < 0.0001$)

relationship between AsV and other species (Fig. 2; Table 3). Clear correlations were obtained because the arsenic source of the subjects was considered to be iAs originating primarily from groundwater. These results were confirmed by the following observations: no arsenic metabolites originating in seafood, including AsBe, TMAO, and AsCho, were detected using HPLC-ICP-MS analysis in any urine samples; there was good agreement

Table 3 Pearson's correlation coefficient between urinary arsenic species

	log(AsIII)	log(AsV)	log(MMA)	log(DMA)	log(iAs[a])	log(iAs + MMA)	log(sumAs[b])
log(AsIII)							
r	1.000	0.654	0.897	0.893	0.988	0.972	0.932
p		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
log(AsV)							
r	0.654	1.000	0.652	0.618	0.737	0.722	0.664
p	<0.001		<0.001	<0.001	<0.001	<0.001	<0.001
log(MMA)							
r	0.897	0.652	1.000	0.902	0.902	0.964	0.935
p	<0.001	<0.001		<0.001	<0.001	<0.001	<0.001
log(DMA)							
r	0.893	0.618	0.902	1.000	0.897	0.921	0.992
p	<0.001	<0.001	<0.001		<0.001	<0.001	<0.001
log(iAs)							
r	0.988	0.737	0.902	0.897	1.000	0.982	0.940
p	<0.001	<0.001	<0.001	<0.001		<0.001	<0.001
log(iAs + MMA)							
r	0.972	0.722	0.964	0.921	0.982	1.000	0.962
p	<0.001	<0.001	<0.001	<0.001	<0.001		<0.001
log(sumAs)							
r	0.932	0.664	0.935	0.992	0.940	0.962	1.000
p	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	

[a] Values are sum of AsIII and AsV

[b] Values are concentrations of sum of arsenic compounds detected in speciation analysis

between tAs and sumAs; urinary sumAs concentration in these subjects was significantly correlated with iAs concentration of drinking water (Table 4); the subjects did not eat seafood according to the questionnaire; and there were no seafood products available in local markets. Buchet et al. [21] report that iAs biotransformation follows first-order rate constants and that urinary metabolites have half-lives ranging from 39 to 59 h. Despite the relatively short half-lives of iAs metabolites, chronic and constant exposure to iAs exhibits steady states of urinary excretion and significant linear relationships between urinary arsenic species. In particular, the very weak correlation between AsIII and AsV was due to the presence of many samples with very low AsV including 106 out of 330 samples that were lower than the detection limit. Since oxidation and reduction always occur in AsIII and AsV [22], and AsIII can oxidize to AsV during sample transport, storage, and preparation [23], iAs is represented by the sum of AsIII and AsV.

Although many studies report arsenic metabolites in the urine of various populations exposed to iAs-contaminated water using HG-AAS analysis [24], only 3 performed urinary arsenic speciation analysis using HPLC-ICP-MS [14, 15, 25]. Furthermore, the number of subjects in our study was larger than those of these 3 studies. Table 6 summarizes the urine of various populations exposed to iAs-contaminated water using HPLC for separation. Five reports describe urinary arsenic speciation analysis using HPLC-HG-AAS [26–30] as shown in Table 6. The proportions of urinary iAs, MMA, and DMA were 11.4–34.0%, 7.5–26.9%, and 47.7–78.8%, respectively. The results of this study are similar to those obtained in a population with 144.7 μgAs/L tAs in West Bengal, India. The proportions are similar to those among various Asian peoples but different from those of Mexicans. Methylation capacity is suggested to differ among ethnicities [24]. The observed difference between Asians and Mexicans is also suggested to be the result of an ethnic difference in methylation capacity.

The correlation coefficient between urinary iAs + MMA concentration and arsenic levels in drinking water is slightly stronger than that between other urinary arsenic species concentrations and arsenic levels in drinking water (Table 4). Total urinary arsenic is commonly used as a biomarker of exposure and is positively correlated with iAs concentration in drinking water in chronically exposed populations [31, 32]. However, in people that eat seafood, significant amounts of tAs are excreted in the urine, including DMA [17, 33, 34]. From the results of the speciation analysis of arsenic in the urine of 172 Japanese

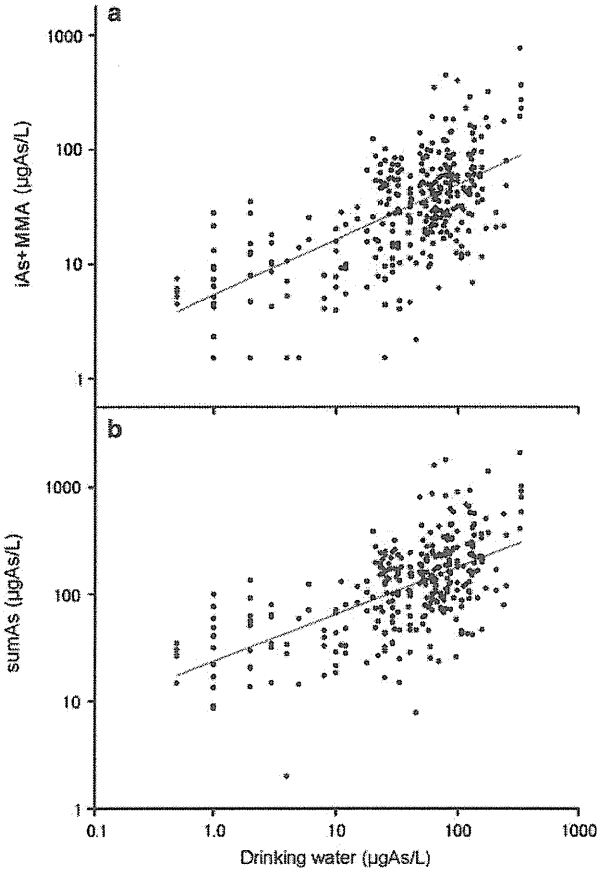

Fig. 3 Scatter plots of the relationships between inorganic arsenic concentrations in drinking water (x) and urinary concentrations (y). **a** y = iAs + MMA, **b** y = sumAs

Table 4 Equations of regression between logarithm of iAs in drinking water (log x) and logarithm of urinary As species (log y)

Urinary species	Equations	r	p value
AsIII	$\log y = 0.470 \log x + 0.442$	0.574	<0.0001
AsV	$\log y = 0.358 \log x - 0.335$	0.495	<0.0001
MMA	$\log y = 0.497 \log x + 0.308$	0.590	<0.0001
DMA	$\log y = 0.420 \log x + 1.264$	0.582	<0.0001
iAs[a]	$\log y = 0.456 \log x + 0.530$	0.597	<0.0001
iAs + MMA	$\log y = 0.474 \log x + 0.744$	0.611	<0.0001
sumAs[b]	$\log y = 0.432 \log x + 1.389$	0.602	<0.0001

[a] Values are sum of AsIII and AsV

[b] Values are concentrations of sum of arsenic compounds detected in speciation analysis

subjects without occupational exposure to iAs, the highest arsenic concentration in urine was for AsBe followed by DMA; these 2 species accounted for about 50 and 30% of tAs, respectively [17, 34]. Among male Italian workers inhaling AsIII, the most excreted species was AsBe, accounting for 34% of the tAs concentration, despite the presence of non-iAs metabolites [35]. In that report, the coefficient of determination between iAs in the air and species present in urine were highest for the sum of iAs, MMA, and DMA ($r^2 = 0.75$) and MMA ($r^2 = 0.75$), but lowest for DMA ($r^2 = 0.53$) [35]. These results clearly show the effects of seafood ingestion on urinary DMA. However, that group did not examine the relationship between iAs in the air and urinary iAs + MMA concentration; instead, they determined the correlation between iAs in the air and urine, and determined that this factor is nearly the same as that between iAs in the air and urinary MMA. Thus, in addition to urinary sumAs concentration, urinary iAs + MMA concentration is a good indicator of iAs exposure. Recently, consumption of seafood has been increasing worldwide. Therefore, the Deutsche Forschungsgemeinschaft (DFG) recommends that only the inorganic arsenic fraction should be determined as the biological tolerance value for iAs exposure in the future [36].

In Fig. 3, urinary iAs + MMA and sumAs concentrations in urine were estimated to be 35.4 and 132.7 μgAs/L, respectively, at 50 μgAs/L of iAs in drinking water. The level is the Bangladeshi standard of iAs in drinking water. Although we did not determine the water intake of the subjects, the average amount of water intake and urinary volume in Bangladeshi adults is reported to be 4 and 2 L/day, respectively [14]. If a subject drinks 4 L water containing 50 μgAs/L, the urinary sumAs concentration would be 70 μgAs/L based on 2 L urine and a 70% excretion rate. However, our results show a nearly 2-fold higher value than this estimation. Since iAs-contaminated groundwater is used extensively to irrigate grains and vegetables, in addition to water, food is also contaminated by iAs in Bangladesh [37–40]. The tAs concentration of Bangladesh rice grains ranges from <0.04 to 1.83 μg/g, and the content of iAs in rice and vegetables is reported to be 87 and 96% of tAs, respectively [37, 40]. It is estimated that an adult Bangladeshi man consumes an average of 1500 g cooked rice per day, which contains approximately 435 g raw rice and at least 1 L water [41]. Meharg and Rahman [37] report that, at 0.5 μgAs/g grain, arsenic contributes to 51% of the dietary arsenic intake for those ingesting 2 L of 0.1 mgAs/L drinking water and 0.42 kg of raw rice. Thus, ingestion of rice is a major source of arsenic exposure in Bangladesh.

For assessing human exposure to arsenic, biomonitoring is a useful tool. Urine is the most frequently used biological medium, and speciating arsenic is important for identifying possible factors that contribute to urinary arsenic levels [42]. Arsenic in hair or fingernail can be a biomarker of long-term arsenic exposure, because inorganic arsenic can bind to sulfhydryl groups in keratin and other proteins in the human body. Limitations of hair or nail monitoring include (1)

Table 5 Effects of BMI, urinary creatinine concentration, and age on proportion of urinary arsenic species and methylation indices among 330 subjects

Item	Pearson's correlation coefficient (r) and probability value (p)				
	iAs[a] (%)	MMA (%)	DMA (%)	PMI	SMI
Total (330)					
log(drinking water)					
r	0.070	0.210	−0.159	0.118	−0.171
p	0.203	0.000	0.004	0.033	0.002
BMI					
r	0.087	−0.142	0.004	−0.162	0.044
p	0.117	0.010	0.942	0.003	0.424
Creatinine					
r	−0.112	−0.002	0.084	0.037	−0.004
p	0.043	0.971	0.126	0.499	0.948
Age					
r	−0.233	0.162	0.093	0.338	−0.059
p	0.000	0.003	0.093	0.000	0.284
Male (165)					
log(drinking water)					
r	0.115	0.315	−0.249	0.196	−0.192
p	0.142	0.000	0.001	0.011	0.013
BMI					
r	0.010	−0.075	0.028	−0.110	0.013
p	0.896	0.338	0.718	0.158	0.873
Creatinine					
r	−0.055	−0.042	0.053	−0.016	0.008
p	0.487	0.590	0.497	0.836	0.915
Age					
r	−0.147	0.061	0.055	0.235	−0.066
p	0.059	0.435	0.483	0.002	0.399
Female (165)					
log(drinking water)					
r	0.043	0.098	−0.080	0.038	−0.148
p	0.582	0.211	0.305	0.627	0.058
BMI					
r	0.095	−0.164	−0.009	−0.159	0.056
p	0.225	0.036	0.913	0.042	0.471
Creatinine					
r	−0.101	−0.051	0.106	−0.009	0.018
p	0.198	0.512	0.176	0.906	0.819
Age					
r	−0.210	0.104	0.127	0.294	0.030
p	0.007	0.185	0.105	0.000	0.698

PMI primary methylation index calculated from urinary MMA/iAs, *SMI* secondary methylation index calculated from urinary DMA/MMA

[a] Values are sum of AsIII and AsV

potential for external contamination, (2) absence of standardized analytical methods, and (3) absence of a well-defined reference range [42]. Therefore, to assess human exposure to iAs, it is essential to determine the arsenic speciation in urine.

In this study, iAs concentration in drinking water ranged from 0.5 to 332 μg/L, and approximately 86% of residents drank water with iAs concentration exceeding the World Health Organization (WHO) reference value of 10 μg/L. Nearly 50% of the population drank water with iAs concentration exceeding 50 μg/L of the Bangladeshi standard (Table 1). This distribution of iAs concentration in drinking water is correlated with that of a large population study in Bangladesh (HEALS); the HEALS study aimed to clarify the health effects of arsenic exposure at low to moderate levels (100–300 μg/L) [43]. Arsenic methylation

Table 6 Urinary arsenic values of various population groups exposed to iAs-contaminated water using HPLC for separation

Study area	Analytical method	*N*	Male (%)	Mean age (range), years		Urinary arsenic					iAs in well water (μgAs/L) or iAs intake (μgAs/day)	Reference
						iAs (%)	MMA (%)	DMA (%)	Others[a] (%)	sumAs[b] (units)		
Bangladesh												
Pabna	HPLC-ICP-MS	330	50.0	37 (20–77)	Median	15.0	11.3	73.7	0.0	126.1 (μgAs/L)	55 μgAs/L	This study
					Mean	15.7	12.4	71.8	0.1	187.7 (μgAs/L)		
Madaripur	HPLC-ICP-MS	24	45.8	32 (13–70)	Mean	18.5	17.2	64.3	–	484.1 (μgAs/L)[c]	372 5 μgAs/L	[14]
Pabna	HPLC-HG-AAS	595	60.3	33.7	Mean	12.8	14.9	73.8	–	51.79 (μgAs/L)[d]	38.0 μgAs/L	[29]
		592	60.3	33.9	Mean	12.9	13.8	72.4	–	147.69 (μgAs/L)	174.0 μgAs/L	
Pabna	HPLC-HG-AAS	195	42.3	33.4 (15–77)	Median	12.6	8.5	78.8	–	30.2 (μgAs/L)[c]	12.5 μgAs/L	[30]
India												
West Bengal	HPLC-ICP-MS	9	50.0	29.1 (8–75)	Mean	11.4	17.4	71.1	–	36.7 (μgAs/L)[c]	2.58 μgAs/L	[25]
		52	55.8	20.2 (3–55)	Mean	17.2	10.7	72.1	–	144.7 (μgAs/L)	6.1 and 25.8 μgAs/L	
		28	50.0	23.9 (5–60)	Mean	34.0	10.5	55.9	–	243.3 (μgAs/L)	36.0 μgAs/L	
Taiwan												
Northeast coast	HPLC-HG-AAS	51	41.2	Male 59.1, female 56.6	Mean	11.7	31.5	56.8	–	113.8 (μgAs/L)[c]	0–50.0 μgAs/L	[26]
		32	43.8		Mean	10.9	24.2	64.9	–	133.4 (μgAs/L)	50.1–299.9 μgAs/L	
		32	40.6		Mean	12.9	22.1	65.0	–	306.5 (μgAs/L)	300–3000 μgAs/L	
Southwestern	HPLC-HG-AAS	26	53.8	63.4	Mean	13.1	16.4	70.5	–	54.5 (μgAs/L)[c]	–	[28]
		26			Mean	11.4	14.6	73.9	–	56.9 (μgAs/L)	–	
Mexico												
Santa Ana, Coahuila	HPLC-HG-AAS	35	–	(22–60)	Mean	30.6	11.3	54.1	–	543.8 (μgAs/g creatinine)[c]	415 μgAs/L	[27]
Cocorit	HPLC-ICP-MS	10	0	36.8 (18–53)	Mean	16.4	15.0	67.1	–	28.0 (μgAs/L)[c]	23.0 μgAs/day	[15]
Col.Allende		10	0	37.1 (22–73)	Mean	22.9	7.5	47.7	–	30.8 (μgAs/L)	14.9 μgAs/day	
Pueblo Yaqui		9	33.3	29.9 (18–58)	Mean	25.4	9.3	55.6	–	31.1 (μgAs/L)	11.9 μgAs/day	
Esperanza		14	21.4	40.2 (19–59)	Mean	24.1	9.7	53.1	–	65.1 (μgAs/L)	65.5 μgAs/day	

– values not described

[a] Values are concentrations of sum of arsenic compounds except inorganic arsenic, MMA, and DMA

[b] Values are sum of concentrations of all arsenic compounds detected in urine by speciation analysis

[c] Values are sum of concentrations of inorganic arsenic, MMA, and DMA

[d] Value is total arsenic concentration directly determined by ICP-MS

capacity is reported to be a risk factor for arsenic-related toxicity because %MMA is most strongly associated with an increased risk of arsenic-induced skin lesions [23, 32]. In our study, iAs in drinking water was significantly positively correlated with the proportions of MMA and PMI, but significantly negatively correlated with the proportions of DMA and SMI in males. However, these correlations were not significant in females (Table 5). These results are concordant with those of previous reports in which PMI was elevated and SMI was depressed in males with high tAs; furthermore, these are related to skin lesions [16, 23, 27, 28, 44]. A significant positive correlation between age and PMI in both males and females in our study is consistent with the results of a report in which older people were more likely to be affected by arsenic exposure [45]. It is reported that urinary creatinine is a predictor of arsenic methylation and higher urinary creatinine concentrations are associated with a reduced risk of skin lesions [23, 46, 47]. Although our subjects exhibited a very wide range of urinary creatinine concentrations, neither PMI nor SMI were associated with urinary creatinine concentrations. Urinary creatinine concentrations were strongly correlated with muscle mass and were affected by red meat intake [20]. There was no correlation between urinary creatinine and BMI among our 330 subjects. Tseng et al. [44] report that BMI is positively correlated with DMA and negatively correlated with MMA. Our results show that BMI is significantly negatively correlated with both MMA (%) and PMI. This result supports the hypothesis that lower BMI is related to the risk of developing skin lesions [45].

The HEALS study included more than 20000 men and women. Chen et al. [32] report that there is little intra-subject variability regarding urinary arsenic metabolite profiles, thus justifying the use of single measurements in epidemiologic studies. In addition, Kile et al. [30] report that, although urinary arsenic ratios are poorly reproducible, urinary arsenic concentrations are fairly reproducible according to the results of longitudinal studies conducted in Bangladesh. Thus, our results apply to residents drinking water with low to moderate levels of arsenic contamination in Bangladesh. Moreover, because seafood ingestion does not affect urinary iAs + MMA concentrations, urinary iAs + MMA concentration is the best indicator of iAs exposure not only in Bangladesh, but for all populations exposed to iAs.

Conclusions

In 330 subjects continuously exposed to iAs who did not ingest seafood, strong correlations and linear regressions among urinary AsIII, AsV, MMA, and DMA were observed over a wide range of concentrations. All urinary species were well correlated with iAs in drinking water, and the most significant linear relationship was obtained between iAs in drinking water and urinary iAs + MMA concentration. Thus, urinary iAs + MMA concentration is a useful biomarker for assessing chronic iAs exposure.

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Conflict of interest The authors have no conflicts of interest to declare.

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平成23年度（第25回）労働衛生検査精度管理調査の実施結果について

労働衛生検査専門委員会
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1．はじめに

公益社団法人全国労働衛生連合会は，健康診断の基礎となる労働衛生検査，臨床検査，胸部エックス線検査の精度の確保・向上を図るため，総合精度管理事業を実施している。労働衛生検査精度管理の実施に当たっては，全衛連に外部の有識者から構成される労働衛生検査専門委員会及び同評価部会を設置して精度管理調査の企画立案，運営管理，評価・分析を行っている。平成19年度から評価法を一部改正し，本年度も改定評価方法（4回目）により評価した。

平成23年度（第25回）労働衛生検査精度管理調査結果の概要を報告する。

2．調査の概要

1）実施時期

試料送付　　平成23年12月5日
報告期限　　平成24年1月10日

2）測定項目

血中鉛量（以下Pb—Bと略す），尿中デルタアミノレブリン酸量（ALA-U），尿中馬尿酸量（HA-U），尿中メチル馬尿酸量（MHA-U），尿中マンデル酸量（MA-U），尿中総三塩化物量（TTC-U），尿中三塩化酢酸量（TCA-U），尿中2,5-ヘキサンジオン量（HD-U），および参考調査として尿中N-メチルホルムアミド（N-MFA-U）

3）参加施設および委託状況

前回と同様，事前に自施設測定か外部委託測定かの調査を行い，全項目を外部委託する施設については試料送付を行わず，1項目でも自施設測定を行う施設（以下「直接参加施設」という。）にのみ試料を送付した。参加施設数は351施設であり，昨年に比べ3施設増加した。参加施設の内，直接参加施設は43施設で，308施設（約88%）については全項目外部委託での参加であった。昨年に比べると，自施設において測定している自施設測定数は1～2施設減少している。測定項目別の参加施設数，自施設測定数，外部施設委託数及び受託施設数は**表1**に示すとおりで，自施設での測定が減少し，検査項目により外部施設への再委託がより進み集約化していた。

表１　参加施設数および自施設測定・委託測定の状況

項目	回	参加施設数（参加率）	自施設検査数（率）	委託施設数（率）	受託施設数
Pb-B	第25回	348　（99.2%）	42　（12.0%）	306　（87.2%）	22
	第24回	344　（98.9%）	45　（12.9%）	299　（85.9%）	20
ALA-U	第25回	348　（99.2%）	42　（12.0%）	306　（87.2%）	22
	第24回	344　（98.9%）	45　（12.9%）	299　（85.9%）	20
HA-U	第25回	350　（99.8%）	42　（12.0%）	308　（87.7%）	22
	第24回	347　（99.7%）	45　（12.9%）	302　（86.8%）	21
MHA-U	第25回	350　（99.8%）	42　（12.0%）	308　（87.7%）	22
	第24回	347　（99.7%）	45　（12.9%）	302　（86.8%）	21
TTC-U	第25回	347　（98.9%）	41　（11.7%）	306　（87.2%）	22
	第24回	343　（98.6%）	44　（12.6%）	299　（85.9%）	19
TCA-U	第25回	343　（97.8%）	39　（11.1%）	304　（86.6%）	21
	第24回	341　（98.0%）	42　（12.1%）	299　（85.9%）	19
MA-U	第25回	348　（99.2%）	42　（12.0%）	306　（87.2%）	22
	第24回	343　（98.6%）	45　（12.9%）	298　（85.6%）	21
HD-U	第25回	350　（99.8%）	42　（12.0%）	308　（87.7%）	22
	第24回	347　（99.7%）	45　（12.9%）	302　（86.8%）	19
N-MFA-U	第25回	346　（98.6%）	40　（11.4%）	306　（87.2%）	22

自施設測定率および委託施設率は，参加施設数を分母とした。

4）試料濃度

試料濃度は自施設測定値の中から異常値を除いた値の平均値を採用した。すなわち，直接参加施設数をNとして平均値と標準偏差SDを計算し，平均値±2SDを超える測定値を除外したのち再度求めた平均をもとに労働衛生検査専門委員会によって最終的に表2のごとく決定された。

5）送付試料の組み合わせ

本年度は**表2**に示すとおり各項目とも6濃度の試料を作製し，直接参加施設へ送付した。

なお，尿中N-メチルホルムアミドについては，参考調査のため，1試料のみ作成・送付している。

3．評価方法

評価項目および評価点は，次のとおりである。

1）解析値評価および許容範囲評価点

評価は各施設から報告されたすべての測定結果を，項目別にまとめ，以下に示す解析値評価（A）と許容範囲評価（B）の2つの方法により実施した。A）解析値評価の配点は，回収率，再現性　，測定バラッキ $\tan\theta$ はそれぞれ満点が6点に，真度PI-1，平均真度I-2はそれぞれ満点が4点で，小計26点と満点なっている。一方，B）測定値範囲評価の配点は個々の測定値が許容される範囲内に納まっているかどうかについて各4点満点の小計24点満点となっている。

表2　第25回クロスチェック（平成23年12月）試料濃度）

記号	項目	試料 (1)	試料 (2)	試料 (3)	試料 (4)	試料 (5)	試料 (6)
A	Pb-B μg/dL	6.8	8.9	15.2	20.5	41.4	43.4
B	ALA-U mg/L	2.6	4.6	7.3	7.6	10.3	11.3
C	HA-U g/L	0.49	0.84	1.19	1.76	2.45	2.51
D	MHA-U g/L	0.25	0.45	0.81	0.91	1.52	1.71
E	TTC-U mg/L	11.6	55.4	100.7	193.9	241.7	324.0
F	TCA-U mg/L	3.3	21.7	43.4	59.9	89.8	115.8
G	MA-U g/L	0.15	0.25	0.46	0.76	1.02	1.23
H	HD-U mg/L	1.3	1.5	2.2	2.7	5.1	5.3
I	N-MFA-U mg/L	19.8					

Pb-B 測定用試料はすべて牛血試料
HD-U　測定試料は人尿試料
その他はすべて人工尿試料
HA-U，MHA-U，MA-U 及び TTC-U，TCA-U　は混合試料

A）解析値評価の種類と評価点

各施設の全測定結果（6試料）について施設ごと，項目別に5種類の計算を行った。

a．方向係数 $Y=a+bX$ の b《回収率》6点

b．ばらつきの程度（再現性）($\sqrt{V_E}$)《再現性》6点

c．測定値を含む確率楕円の長軸の傾きの正切（$\tan\theta$)《測定バラッキ》6点

d．パフォーマンス・インデックス1（PI-1）《真度》4点

e．パフォーマンス・インデックス2（PI-2）《平均真度》4点

B）測定値の許容範囲に対する評価点

個々の測定値が許容される範囲内に納まっているかどうかについて，各試料4点満点，小計24点（6試料×4点）とした。

①　試料毎の試料濃度に対する標準偏差

まず各測定項目について，濃度の同じ試料ごとに自施設で測定した測定値 n(1) を累計し，平均値 AVE(1) に対する標準偏差 SD(1) を求めた。次いで AVE(1) ± 2 SD を超える測定値を異常値として除外し，AVE(1) ± 2SD の範囲内にある測定値 n(2) により，あらためて平均値(試料濃度とする) AVE(2) と標準偏差 SD(2) を計算し，測定値に対する評価に際しての SD(2) とした。なお，第25回(平成23年度）労働衛生検査精度管理調査における全参加施設（43施設）から求めた各試料(n(1)，n(2)) に対する平均値(AVE(1)，AVE(2)(試料濃度)) と標準偏差(SD(1)，SD(2)) を**表3**に示した。

②　測定値に対する評価

測定値に対する評価は，「鉛および有機溶剤健康診断結果報告のための分布区分」に従い，各項目の分布1，2，3毎に決定した。低濃度（分布1）と高濃度（分布3）の試料に対しては労働衛生検査専門委員会が絶対的許容範囲を設定し，中濃度（分布2）の試料に対しては試料濃度の± 10%という相対的許容範囲とした。なお，本年度配布試料の許容される濃度範囲とその評価点数の関係を**表4**に示した。

C）総合点評価

解析値評価法における5種類の評価点（小計

表3　直接参加施設（43 施設）から求めた各試料の平均値（試料濃度）及び標準偏差

項　目		試料 1	試料 2	試料 3	試料 4	試料 5	試料 6
Pb-B	n（1）	42	42	42	42	42	42
	AVE（1）	6.9	8.9	15.2	20.5	41.3	43.3
	SD（1）	0.25	0.28	0.32	0.50	0.94	1.16
	n（2）	39	41	40	39	39	39
	AVE（2）	6.8	8.9	15.2	20.5	41.4	43.4
	SD（2）	0.19	0.25	0.29	0.42	0.77	0.90
ALA-U	n（1）	42	42	42	42	42	42
	AVE（1）	2.6	4.6	7.3	7.6	10.3	11.3
	SD（1）	0.09	0.13	0.19	0.20	0.29	0.33
	n（2）	42	40	41	39	40	41
	AVE（2）	2.6	4.6	7.3	7.6	10.3	11.3
	SD（2）	0.09	0.10	0.16	0.13	0.23	0.28
HA-U	n（1）	42	42	42	42	42	42
	AVE（1）	0.49	0.84	1.19	1.76	2.45	2.51
	SD（1）	0.01	0.01	0.03	0.03	0.05	0.06
	n（2）	40	40	39	40	38	39
	AVE（2）	0.49	0.84	1.19	1.76	2.45	2.51
	SD（2）	0.01	0.01	0.01	0.03	0.03	0.03
MHA-U	n（1）	42	42	42	42	42	42
	AVE（1）	0.26	0.44	0.81	0.93	1.52	1.68
	SD（1）	0.03	0.03	0.03	0.13	0.04	0.14
	n（2）	41	41	40	41	39	41
	AVE（2）	0.25	0.45	0.81	0.91	1.52	1.71
	SD（2）	0.01	0.01	0.01	0.03	0.02	0.04
TTC-U	n（1）	41	41	41	41	41	41
	AVE（1）	11.5	55.2	100.3	192.9	241.7	323.4
	SD（1）	0.49	2.31	2.17	5.58	5.94	9.19
	n（2）	39	40	36	39	41	40
	AVE（2）	11.6	55.4	100.7	193.9	241.7	324.0
	SD（2）	0.42	2.18	1.25	3.24	5.94	8.68
TCA-U	n（1）	39	39	39	39	39	39
	AVE（1）	3.3	21.8	43.4	59.6	89.8	115.8
	SD（1）	0.14	0.65	1.78	1.41	2.81	3.47
	n（2）	39	38	39	36	39	39
	AVE（2）	3.3	21.7	43.4	59.9	89.8	115.8
	SD（2）	0.14	0.49	1.78	0.95	2.81	3.47
MA-U	n（1）	42	42	42	42	42	42
	AVE（1）	0.15	0.25	0.46	0.76	1.02	1.23
	SD（1）	0.01	0.01	0.01	0.01	0.02	0.03
	n（2）	41	40	40	39	42	40
	AVE（2）	0.15	0.25	0.46	0.76	1.02	1.23
	SD（2）	0.01	0.01	0.01	0.01	0.02	0.02
HD-U	n（1）	42	42	42	42	42	42
	AVE（1）	1.3	1.5	2.2	2.7	5.1	5.3
	SD（1）	0.10	0.10	0.13	0.15	0.19	0.16
	n（2）	41	41	41	42	41	41
	AVE（2）	1.3	1.5	2.2	2.7	5.1	5.3
	SD（2）	0.09	0.09	0.12	0.15	0.18	0.15
N-MFA-U	n（1）	40					
	AVE（1）	19.8					
	SD（1）	0.76					
	n（2）	39					
	AVE（2）	19.8					
	SD（2）	0.72					

n（1）：集計件数　AVE（1）：n（1）による試料平均濃度　SD（1）：n（1）による標準偏差
n（2）：異常値を除いた集計件数　AVE（2）：n（2）による試料平均濃度　SD（2）：n（2）による標準偏差

表4　項目別試料濃度別の評価点数に対応する濃度範囲

項　目	点数	試料-1	試料-2	試料-3	試料-4	試料-5	試料-6
Pb-B μg/dL	試料濃度	6.8μg/dL	8.9μg/dL	15.2μg/dL	20.5μg/dL	41.4μg/dL	43.4μg/dL
	4点	±2.0μg/dL以内	±2.0μg/dL以内	±2.0μg/dL以内	±2.05μg/dL以内	±4.0μg/dL以内	±4.0μg/dL以内
	3点	±3.0μg/dL以内	±3.0μg/dL以内	±3.0μg/dL以内	±3.08μg/dL以内	±6.0μg/dL以内	±6.0μg/dL以内
	2点	±4.0μg/dL以内	±4.0μg/dL以内	±4.0μg/dL以内	±4.10μg/dL以内	±8.0μg/dL以内	±8.0μg/dL以内
ALA-U mg/L	試料濃度	2.6mg/L	4.6mg/L	7.3mg/L	7.6mg/L	10.3mg/L	11.3mg/L
	4点	±0.5mg/L以内	±0.5mg/L以内	±0.73mg/L以内	±0.76mg/L以内	±1.0mg/L以内	±1.0mg/L以内
	3点	±0.75mg/L以内	±0.75mg/L以内	±1.10mg/L以内	±1.14mg/L以内	±1.5mg/L以内	±1.5mg/L以内
	2点	±1.0mg/L以内	±1.0mg/L以内	±1.46mg/L以内	±1.52mg/L以内	±2.0mg/L以内	±2.0mg/L以内
HA-U g/L	試料濃度	0.49g/L	0.84g/L	1.19g/L	1.76g/L	2.45g/L	2.51g/L
	4点	±0.1g/L以内	±0.1g/L以内	±0.12g/L以内	±0.18g/L以内	±0.25g/L以内	±0.25g/L以内
	3点	±0.15g/L以内	±0.15g/L以内	±0.18g/L以内	±0.26g/L以内	±0.37g/L以内	±0.375g/L以内
	2点	±0.2g/L以内	±0.2g/L以内	±0.24g/L以内	±0.35g/L以内	±0.49g/L以内	±0.5g/L以内
MHA-U g/L	試料濃度	0.25g/L	0.45g/L	0.81g/L	0.91g/L	1.52g/L	1.71g/L
	4点	±0.05g/L以内	±0.05g/L以内	±0.08g/L以内	±0.09g/L以内	±0.15g/L以内	±0.15g/L以内
	3点	±0.075g/L以内	±0.075g/L以内	±0.12g/L以内	±0.14g/L以内	±0.225g/L以内	±0.225g/L以内
	2点	±0.1g/L以内	±0.1g/L以内	±0.16g/L以内	±0.18g/L以内	±0.3g/L以内	±0.3g/L以内
TTC-U mg/L	試料濃度	11.6mg/L	55.4mg/L	100.7mg/L	193.9mg/L	241.7mg/L	324.0mg/L
	4点	±5.0mg/L以内	±5.54mg/L以内	±10.07mg/L以内	±19.39mg/L以内	±24.17mg/L以内	±30.0mg/L以内
	3点	±7.5mg/L以内	±8.30mg/L以内	±15.11mg/L以内	±29.09mg/L以内	±36.26mg/L以内	±45.0mg/L以内
	2点	±10.0mg/L以内	±11.07mg/L以内	±20.15mg/L以内	±38.79mg/L以内	±48.34mg/L以内	±60.0mg/L以内
TCA-U mg/L	試料濃度	3.3mg/L	21.7mg/L	43.4mg/L	59.9mg/L	89.8mg/L	115.8mg/L
	4点	±3.0mg/L以内	±3.0mg/L以内	±4.34mg/L以内	±5.99mg/L以内	±8.98mg/L以内	±10.0mg/L以内
	3点	±4.5mg/L以内	±4.5mg/L以内	±6.51mg/L以内	±8.99mg/L以内	±13.48mg/L以内	±15.0mg/L以内
	2点	±6.0mg/L以内	±6.0mg/L以内	±8.68mg/L以内	±11.98mg/L以内	±17.97mg/L以内	±20.0mg/L以内
MA-U g/L	試料濃度	0.15g/L	0.25g/L	0.46g/L	0.76g/L	1.02g/L	1.23g/L
	4点	±0.03g/L以内	±0.03g/L以内	±0.05g/L以内	±0.08g/L以内	±0.1g/L以内	±0.1g/L以内
	3点	±0.045g/L以内	±0.045g/L以内	±0.07g/L以内	±0.11g/L以内	±0.15g/L以内	±0.15g/L以内
	2点	±0.06g/L以内	±0.06g/L以内	±0.09g/L以内	±0.15g/L以内	±0.2g/L以内	±0.2g/L以内
HD-U mg/L	試料濃度	1.3mg/L	1.5mg/L	2.2mg/L	2.7mg/L	5.1mg/L	5.3mg/L
	4点	±0.2mg/L以内	±0.2mg/L以内	±0.22mg/L以内	±0.27mg/L以内	±0.5mg/L以内	±0.5mg/L以内
	3点	±0.3mg/L以内	±0.3mg/L以内	±0.32mg/L以内	±0.41mg/L以内	±0.75mg/L以内	±0.75mg/L以内
	2点	±0.4mg/L以内	±0.4mg/L以内	±0.43mg/L以内	±0.55mg/L以内	±1.0mg/L以内	±1.0mg/L以内

小数点3位以下は切捨てた。

26点満点）と許容範囲評価での6資料の評価点（小計24点満点）を合計した50点満点を，100点満点に換算した。さらに，血中鉛と尿中デルタアミノレブリン酸の評価点の平均を鉛平均，有機溶剤代謝物の評価点の平均を有機平均として算出し，鉛平均と有機平均の平均を全平均（総合点）とした。

4．間接参加施設の評価結果について

昨年度と同様に自施設で測定を行わない項目については，通常測定委託する外部施設に測定結果を問い合わせ，その値を委託測定分として報告をしてもらった。そこで，委託された外部施設の評価結果についてまとめた。

外部施設への委託率は表1に示すとおり87%前後であり，委託率が比較的高い検査項目のHA-U，MHA-UおよびHD-U（95.1%）は87.7％，委託率が最も低いTCA-Uで86.6%であった。一方，自施設検査数および自施設検査率は昨年度に比べ減少している。

1）受託外部施設数

各項目の受託施設数は表1に示すとおりであるが，これら外部施設のうち6施設で全体の検査数の85%以上を受託している。

2）受託外部施設の測定結果

本年度の試料を送付した施設は43施設である。なお，直接参加43施設の中には項目の一部について再委託している施設が含まれており，項目別評価の自施設測定施設数が最大42施設となっている。参加施設の報告値を測定散布図として報告値（Xi－AVE(1)）／AVE(1)の%で表したものを**図1**の①～⑧に示した。図中の平均値は異常値を除いた全測定値（n(1)の平均値（AVE(1)）で±30%を超えた値は×で表示した。

3）受託外部施設の評価結果

外部委託分の評価点別施設数及び外部施設の評価結果は**表5**および**表6**に示すとおりである。

5．測定方法別評価合計点について

今回の結果報告では次の測定方法は用いられていた。Pb―Bについては全施設ともフレームレス原子吸光法を採用しており，ALA-Uについては緒方一友国法を採用しているのが4施設，他の施設は液体クロマトグラフ法であった。また，HA-U，MHA-U，MA-Uについては全施設液体クロマトグラフ法を採用している。TTC-U，TCA-Uについても大部分が液体クロマトグラフ法で，吸光々度法が3施設，GC-MS法が2施設であった。また，HD-Uについてはガスクロマトグラフ法が27施設，GC-MS法が15施設であった（詳細は，平成23年度労働衛生検査精度管理調査結果報告書31p～33pを参照されたい）。なお，測定方法別による集計結果に有意差が見られないことから表4の濃度範囲に準じて評価した。

6．評価結果

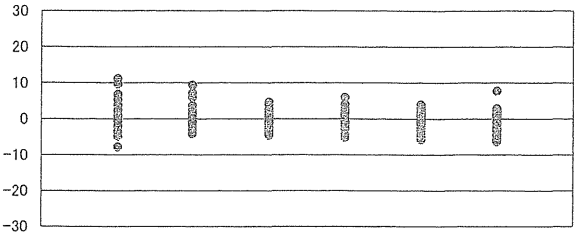
1）外部委託施設の項目ごとの評価

本年度外部委託施設における各項目の評価点別ごとの施設数を表5に示した。なお，測定上の問題点や評価点の低い施設の結果に対するコメント等は平成23年度報告書に解説を記しているので参照願いたい。

2）総合評価

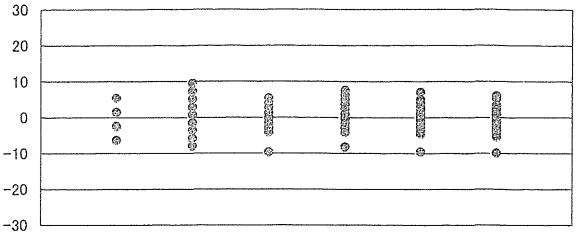
平成16年度より全衛連が実施する労働衛生検査精度管理調査結果は公表することとな

(%)　血中鉛量(Pb－B)　（参加機関数：42）



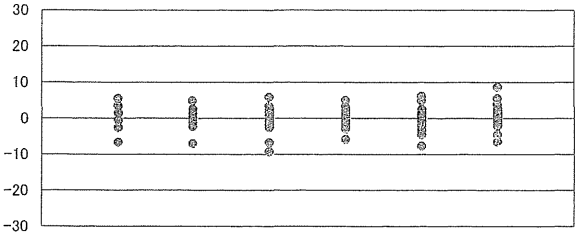
	試料1	試料2	試料3	試料4	試料5	試料6
平均	6.9	8.9	15.2	20.5	41.3	43.3
SD	0.25	0.28	0.32	0.50	0.94	1.16
最大値	7.6	9.7	15.9	21.7	43.0	46.7
最小値	6.3	8.5	14.5	19.4	39.0	40.6

(%)　尿中デルタアミノレブリン酸量(ALA-U)（参加機関数：42）



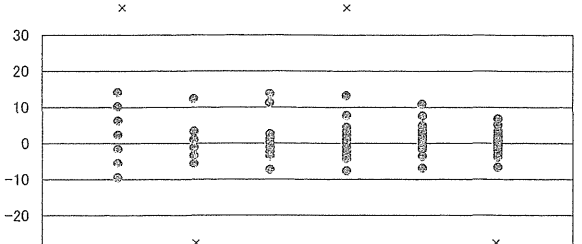
	試料1	試料2	試料3	試料4	試料5	試料6
平均	2.6	4.6	7.3	7.6	10.3	11.3
SD	0.09	0.13	0.19	0.20	0.29	0.33
最大値	2.7	5.0	7.7	8.2	11.0	12.0
最小値	2.4	4.2	6.6	7.0	9.3	10.2

(%)　尿中馬尿酸量(HA-U)　（参加機関数：42）



	試料1	試料2	試料3	試料4	試料5	試料6
平均	0.49	0.84	1.19	1.76	2.45	2.51
SD	0.01	0.01	0.03	0.03	0.05	0.06
最大値	0.52	0.88	1.26	1.84	2.60	2.72
最小値	0.46	0.78	1.08	1.65	2.26	2.34

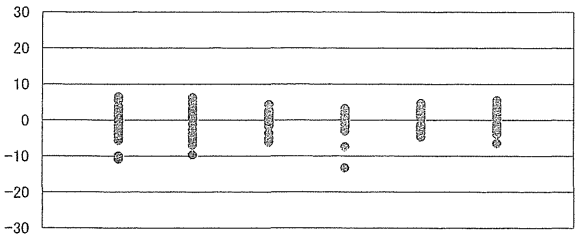
(%)　尿中メチル馬尿酸量(MHA-U)　（参加機関数：42）



	試料1	試料2	試料3	試料4	試料5	試料6
平均	0.26	0.44	0.81	0.93	1.52	1.68
SD	0.03	0.03	0.03	0.13	0.04	0.14
最大値	0.45	0.50	0.92	1.72	1.68	1.82
最小値	0.23	0.25	0.75	0.84	1.41	0.81

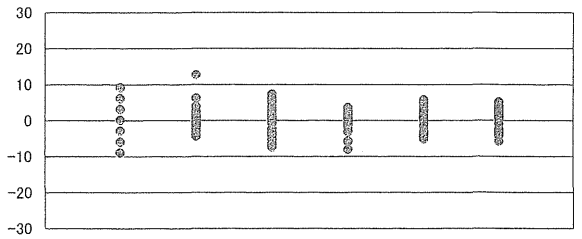
※30%もしくは－30%を超えている場合は【×】が表示されています。

(%)　尿中総三塩化物量(TTC-U)　（参加機関数：41）



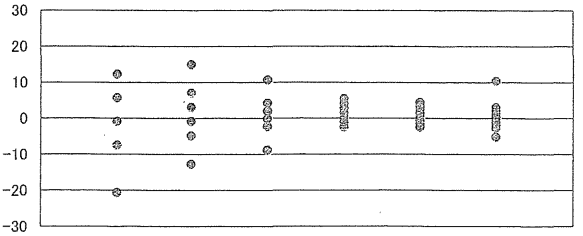
	試料1	試料2	試料3	試料4	試料5	試料6
平均	11.5	55.2	100.3	192.9	241.7	323.4
SD	0.49	2.31	2.17	5.58	5.94	9.19
最大値	12.3	58.7	104.9	199.7	252.4	340.8
最小値	10.3	49.9	94.4	167.7	229.9	302.5

(%)　尿中トリクロル酢酸量(TCA-U)　（参加機関数：39）



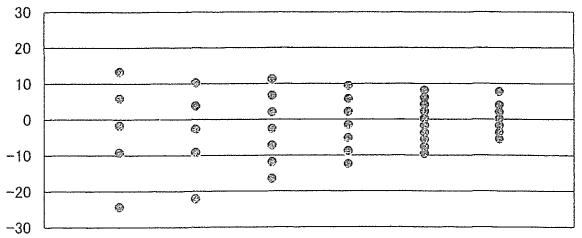
	試料1	試料2	試料3	試料4	試料5	試料6
平均	3.3	21.8	43.4	59.6	89.8	115.8
SD	0.14	0.65	1.78	1.41	2.81	3.47
最大値	3.6	24.4	46.5	62.0	94.9	121.6
最小値	3.0	20.7	40.1	55.0	85.1	108.9

(%)　尿中マンデル酸量(MA-U)　（参加機関数：42）



	試料1	試料2	試料3	試料4	試料5	試料6
平均	0.15	0.25	0.46	0.76	1.02	1.23
SD	0.01	0.01	0.01	0.01	0.02	0.03
最大値	0.17	0.29	0.51	0.80	1.06	1.35
最小値	0.12	0.22	0.42	0.74	0.99	1.16

(%)　尿中2,5-ヘキサンジオン量(HD-U)　（参加機関数：42）



	試料1	試料2	試料3	試料4	試料5	試料6
平均	1.3	1.5	2.2	2.7	5.1	5.3
SD	0.10	0.10	0.13	0.15	0.19	0.16
最大値	1.5	1.7	2.4	3.0	5.5	5.7
最小値	1.0	1.2	1.8	2.4	4.6	5.0

※30%もしくは－30%を超えている場合は【×】が表示されています。

図１　直接参加施設の検査項目別偏差（散布図）

表5　外部委託施設の評価点別施設数

評価点	Pb-B		ALA-U		HA-U		MHA-U	
100～85	306	100.0%	306	100.0%	308	100.0%	308	100.0%
85～70	0	0.0%	0	0.0%	0	0.0%	0	0.0%
70～60	0	0.0%	0	0.0%	0	0.0%	0	0.0%
59～0	0	0.0%	0	0.0%	0	0.0%	0	0.0%
評価点	TTC-U		TCA-U		MA-U		HD-U	
100～85	306	100.0%	304	100.0%	305	99.7%	307	99.7%
85～70	0	0.0%	0	0.0%	0	0.0%	1	0.0%
70～60	0	0.0%	0	0.0%	0	0.0%	0	0.0%
59～0	0	0.0%	0	0.0%	1	0.3%	0	0.3%

表6　全参加施設の総合評価点によるランク一覧

ランク	平成23年度 全参加機関数	比率（%）	平成22年度 全参加機関数	比率（%）	平成21年度 全参加機関数	比率（%）
A（評価合計点の平均が85点以上）	351	100.0	347	99.7	334	98.5
B（評価合計点の平均が70点以上85点未満）	0	0.0	1	0.3	2	0.6
C（評価合計点の平均が60点以上70点未満）	0	0.0	0	0.0	0	0.0
D（評価合計点の平均が60点未満）	0	0.0	0	0.0	5	1.5

り，評価合計点の平均が85点以上の評価区分を「評価A」，70点以上85点未満を「評価B」，60点以上70点未満を「評価C」，60点未満を「評価D」とした。そして，「評価A」は「優」，「評価B，C」は「良」と表示して全衛連ホームページ等に公表することとなった。

総合評価の各ランクの施設数を表6に示したが，本調査では全ての施設がAランクとなった。

7．まとめ

第25回をむかえた労働衛生検査の精度管理調査も生体試料測定クロスチェックとその評価を行い終了した。参加施設はここ数年微増しており，今年度の参加申し込み機関は351施設（平成22年度348施設）であった。この351の参加施設の全ての施設が総合評価Aであり，生体試料の分析は精度管理が十分に行なえていると判断する。

ただ，総合評価がAであっても，各項目別にみると，ALA，MHA，MA，HDではB評価，C評価の施設がいくつかあり，各項目別評価の低い施設においては，溶液の標準濃度の作成方法，希釈方法，波長測定等の分析条件の確認が必要であると考える。

今回もHD-U用試料には分析時のクロマト解析に影響を与える可能性のある2-アセチル

フランが 1mg/L 添加されていたが，HD-U の評価点は直接参加施設 42 施設中 39 施設が 85 点以上であった。

成績の公表については，参加全項目の平均による総合評価の成績を点数ではなく，A（100～85 点），B（70～85 点未満），C（60～70 点未満），D（60 点未満）で公表することにした。

これは，わずかな点数の違いが，実際には問題とする必要がないにも係らず，精度管理および営業上不必要な悪影響を及ぼしているからである。

なお，各評価の内容は次の如く考えて欲しい。

A：技術的に良好でこの状態を維持する努力をして欲しい。

B：技術的に良好な状態にするため努力をして欲しい。

C：技術的に良好な状態にするため，一層の努力をして欲しい。

D：技術的に不十分であり，早急な対策と努力が必要である。

一方，外部施設に委託している施設は，委託先の成績をその施設の成績としたが，良い結果が得られなかった施設は委託先と十分話し合いをされることが必要と考える。また，引き続いて委託される場合には委託先を充分監視できる体制を整える必要があろう。受託施設ではその使命上，全ての項目で 90 点以上を取ってほしいと考えている。

例年のことであるが本年度の報告においても，記載ミス，計算間違いなどにより成績の悪かった施設が見受けられた。記載ミスはヒューマンエラーの典型例であり，人間の認知，行動の失敗と捉え，心理学からのアプローチがいちばん有効と考えられている。労働の安全，衛生，保健に従事する者が最初に取り組むべき課題である。

外部施設に委託している施設においても，転記時のダブルチェックなど，健康診断におけるヒューマンエラー対策を外部制度管理のひとつとして実施することを提案する。

最後に次回も数多くの施設が参加され，優秀な成績を上げられることを期待する。